



## An evaluation of the safety of blood product transfusion in children under 18: systematic review

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### Evidence in Context

**Prior Evidence:** Blood transfusions in children are common but risky procedures. Previous studies have reported various types of acute and late adverse effects, such as allergic, haemolytic, bacterial, and lung reactions. However, the exact frequency, severity, and causes of these reactions are not well established. More research and surveillance are needed to improve the safety and efficacy of transfusion therapy in paediatrics.

**Evidence added by this study:** This systematic review addressed the transfusion responses in paediatrics and the increasing transfusion reactions in children. It advocates more clinical trials to ascertain the safety of blood transfusion in children. It demonstrates that the current evidence does not support the safety of transfusion triggers, and emphasizes the necessity for further research to offer other approaches for preventing detrimental acute responses in children who require transfusions.

### To view Article



### Abstract

**Background:** Every year, blood transfusions save countless lives, extend life expectancy, enhance the condition of life of individuals with life-threatening illnesses. The rate of blood transfusion reactions in children is higher than in the general population of adults. As children grow and develop, they are very different from adults regarding how they need to be diagnosed and treated.

**Objective:** The systematic review aimed to evaluate potential adverse consequences and correlations associated with blood transfusions in children.

**Methods:** A literature search was carried out using PubMed, Scopus, Embase, MEDLINE, CINAHL, Web of Science, and Cochrane. A manual search was also undertaken using reference harvesting in ARU. The literature search was done to cover the duration between 2011 to 2021 using Boolean logic with the following terms: Blood transfusion, Transfusion Safety, Adverse effects/Transfusion, Transfusion reaction, and Children.

**Results:** The majority of the studies discussed RBC transfusion among critically ill children. They all reach an almost similar opinion that there are adverse effects associated with blood transfusion, especially in immunocompromised children or neonates. Discussions about plasma transfusions also showed the same results. The significant outcomes of the blood transfusion are nosocomial infections, prolonged hospital stay, early mortality, and transfusion-related hyperkalaemia. Although transfusion is a valuable therapy, there is always the possibility of side effects, with a greater occurrence rate in children under the age of 18, thus the healthcare team must respond quickly to minimise problems and control those that do occur.

**Conclusions:** Acute and chronic diseases usually necessitate blood transfusions. This systematic study emphasises paediatric transfusion responses and shows that the incidence of transfusion reactions among the paediatric population is on the rise. More research is necessary to explain suitable indications and the introduction of standardised protocols for the blood transfusion process and subsequent reactions in children.

**Keywords:** Blood transfusion, Safety, Transfusion reaction, Children, Paediatric transfusion, Haemovigilance, Paediatrics, Adolescents, Infants, Evidence synthesis

## Background

Every year, blood transfusions save countless lives, extend life expectancy, enhance the condition of life of individuals with life-threatening illnesses, and aid in completing complicated medical and surgical operations [1]. When unsafe blood is available for transfusion, it has a detrimental influence on the performance of essential health services and programmes responsible for providing proper patient treatment in an extensive variety of acute and chronic illnesses [1]. Worldwide, over 112 million units of blood are processed each year, with approximately 14 million units of blood transfused each year [2].

It is possible to make efficient use of blood if it is separated into different products such as red cell concentrates, platelet concentrates, plasma, and cryoprecipitates, which will meet the requirements of more than one patient [1]. Red blood cells are transfused into patients to increase their oxygen-carrying capability [3]. In individuals with clinically substantial coagulopathy, plasma transfusion can help restore their health [3]. Patients with thrombocytopenia or platelet dysfunction benefit from transfused platelets because they can prevent or control bleeding [3]. The transfusion of cryoprecipitate is used to treat hypofibrinogenemia [3].

Transfusions are often required in paediatrics, notably in preterm infants, patients with hematologic malignancies or diseases, and severely unwell children in paediatric intensive care units [4]. Paediatric patients admitted to high-risk critical care units are about 5% more likely than the general population to get at least one transfusion during their stay [5].

During their growth and development, children differ significantly from adults. They have a unique set of needs that must be considered when making decisions about the type of product, alteration, dosages, rate of administering, and possible side effects of blood transfusions [6-8].

In spite of the progress in transfusion safety accomplished through the application of good manufacturing practise (GMP) and ideal treatment protocols, formed elements can cause acute (within 24 hours) or delayed (within 24 hours) adverse effects, particularly in transfusion-dependent paediatric patients [9]. The consequences of a transfusion process may directly impact a child's long-term health, particularly in the case of neurocognitive development in children [10]. The nature and severity of harmful transfusion responses in children who have received blood transfusions differ from those in adults [11]. It is almost transparent that studies showing a reduced utilisation of blood transfusion may be attributed to a positive impact on patient surgical treatment and policies advocating the sensible use of donated blood products in the first place [12,13].

A comprehensive understanding of the many forms of adverse transfusion reactions and their prevalence in this paediatric group is required. However, this remains a considerable problem. Innovative research studies and active hemovigilance are necessary to enhance screening, increase the detection of adverse transfusion events, and encourage the use of new procedures and preventative strategies in clinical practice, all of which will benefit patients [11].

Adverse transfusion responses in children continue to be poorly understood and discussed. How often and in what order unfavourable reactions to blood transfusions occur is still unclear. Uncertainty about the actual nature of the hazards and benefits of blood transfusion can lead to reports of considerable differences in the transfusion technique in children with various blood products. The systematic review aimed to evaluate potential adverse consequences and correlations associated with blood transfusions in children.

## Material and Methods

### Study Design

This study was designed to provide an inclusive picture of blood transfusion reactions in children. It systematically searched the medical literature and identified all the relevant publications comparing blood transfusion safety in children. It included quantitative observational studies reporting original research evidence on this topic.

### Search Strategy

Following the guidelines published by the Centre for Reviews and Dissemination (CRD) in 2009, an initial evaluation of the current literature was conducted to substantiate this systematic review's necessity. The first assessment of the literature was conducted using the databases PubMed, CINAHL Plus, Embase, Scopus, MEDLINE, and Web of Science. After that, the Cochrane Database of Systematic Reviews (CDSR) was searched for any existing or current systematic reviews conducted at the search time. Various systematic reviews on blood product transfusion and its adverse effects were identified; however, no systematic review studied blood transfusion safety in the paediatric age group or children under 18.

A complete search of the published literature was carried out per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [14]. The search for relevant literature was not restricted to a particular country. It was conducted on several databases to prevent missing important research and reduce bias. The searched databases were PubMed,

CINAHL Plus, Embase, Scopus, MEDLINE, Web of Science and Cochrane Library, electronically to obtain relevant research studies published from 1st January 2011 to 31st April 2021. A second step was to manually check the reference lists of the currently qualified research to guarantee that no eligible studies were overlooked. The search technique will integrate just terms representing to and referring the participants and the intervention.

The search strategy follows the PICOTT framework [15] (Population, Intervention, Comparator, Outcome, Type of Question, Type of Study) to identify the keywords due to their suitability to assess clinical questions, especially to identify therapy/ intervention effectiveness [16] (Table 1).

**Table 1. PICOTT framework**

P – Population/Participants	Children who received at least one blood product transfusion. Definition of group: Children
I – Intervention	Blood product or whole blood transfusion
C – Comparator	Whole blood transfusion to no transfusion
O – Outcome	Mortality associated with receipt of blood transfusion (hyperkalemia) Transfusion-transmitted infection Complications during the hospital stay Metabolic complications
T – Type of Question	Prognosis type
T – Type of Study	Interventional and Non-interventional studies; Observational Studies

The search of databases found 4739 articles, and 6 papers were found by harvesting references (Figure 1). Boolean operators combinations and truncations were utilised to narrow down the search results. The MeSH browser was utilised to index articles. The keywords that were used to search the databases were: “Blood transfusion” and “Transfusion Safety” or “Adverse effects/Transfusion” or “Transfusion reaction” and “Whole blood transfusion” or “Red blood cell transfusion” or “Platelet transfusion” or “Plasma transfusion” or “granulocyte transfusion” and “Pediatrics” or “Children” or “Infants” either singly or in combination. With the implementation of search limitations, the scope of the search was narrowed to include only primary peer-reviewed papers that were available in the English language and full-text articles.

**Study Selection**

The inclusion and exclusion criteria are listed in Table 2:

**Table 2. PICOTT framework**

	Inclusion Criteria	Exclusion Criteria
P – Population/Participants	Children Children who received at least one blood product transfusion.	All others above 18 years of age Children who didn’t receive any unit of blood transfusion
I – Intervention	Blood product or whole blood transfusion	Articles did not collect data on blood transfusion
C – Comparator	Whole blood transfusion to no transfusion	Alternative therapies (blood substitutes)
O – Outcome	Mortality following blood transfusion Complications during the hospital stay Metabolic complications (hyperkalemia) Transfusion-transmitted infection	The articles did not collect data regarding the blood transfusion reactions
T – Type of Question	Prognosis type	All articles did not collect data regarding the prognosis-type question
T – Type of Study	Interventional studies Non-interventional studies Observational Studies Articles in the English Language Literature completed after 2011	Meta-analyses and systematic review Case studies with less than 10 participants Articles other than in the English language Literature completed prior to 2011

Before applying the inclusion and exclusion criteria, the duplicated papers were eliminated using the RefWorks tool and manually reviewed to ensure no bias caused by duplication. A total of 4349 publications were found in the literature search after the duplicate articles were removed, and a total of 06 studies were obtained through reference harvesting (Fig 1). 3963 records excluded after title screening. 386 reports were sought for retrieval.

Inclusion Criteria and Exclusion Criteria Implementation:

The papers found as an outcome of the search were screened for research design in the first step. After that, the title and abstract of each search result were screened using “P” “I” “C” “O” “T” “T” inclusion and exclusion criteria for sample and research designs that were limited to interventional and non-interventional studies and observational studies. From the literature search, it was found that in some articles, the population group was not children, and alternative therapies were used as intervention instead of blood transfusion. In the next phase of screening, 82 relevant articles on blood transfusion (I-intervention) in children (P-Population) resulted from the search. Their full-text articles were scanned for data collected from participants regarding Blood transfusion or not (C-Comparator) and searched for complications and mortality after blood transfusion (O-Outcome). Articles that provided insufficient or unfocused information regarding blood transfusion were excluded. After implementing the inclusion and exclusion criteria, 12 papers were chosen for the critical appraisal stage (Figure 1 & Table 2).

**Critical Appraisal**

Various evaluation techniques were used to evaluate the research. Twelve papers were assessed using two critical evaluation techniques to investigate the studies’ methodological strengths and flaws as well as their validity and reliability. It was also carried out to determine if the studies had been developed, conducted, and documented adequately and whether they produced a relevant answer to the systematic review issue in question. The cross-sectional study was evaluated using the Appraisal Tool for

Cross-Sectional Studies (AXIS) [17], specifically intended to assess this design. The prospective or retrospective study's quality assessment was conducted using the CASP tool [18]. After the quality check, one study [19] was removed as no definitive conclusion was drawn.

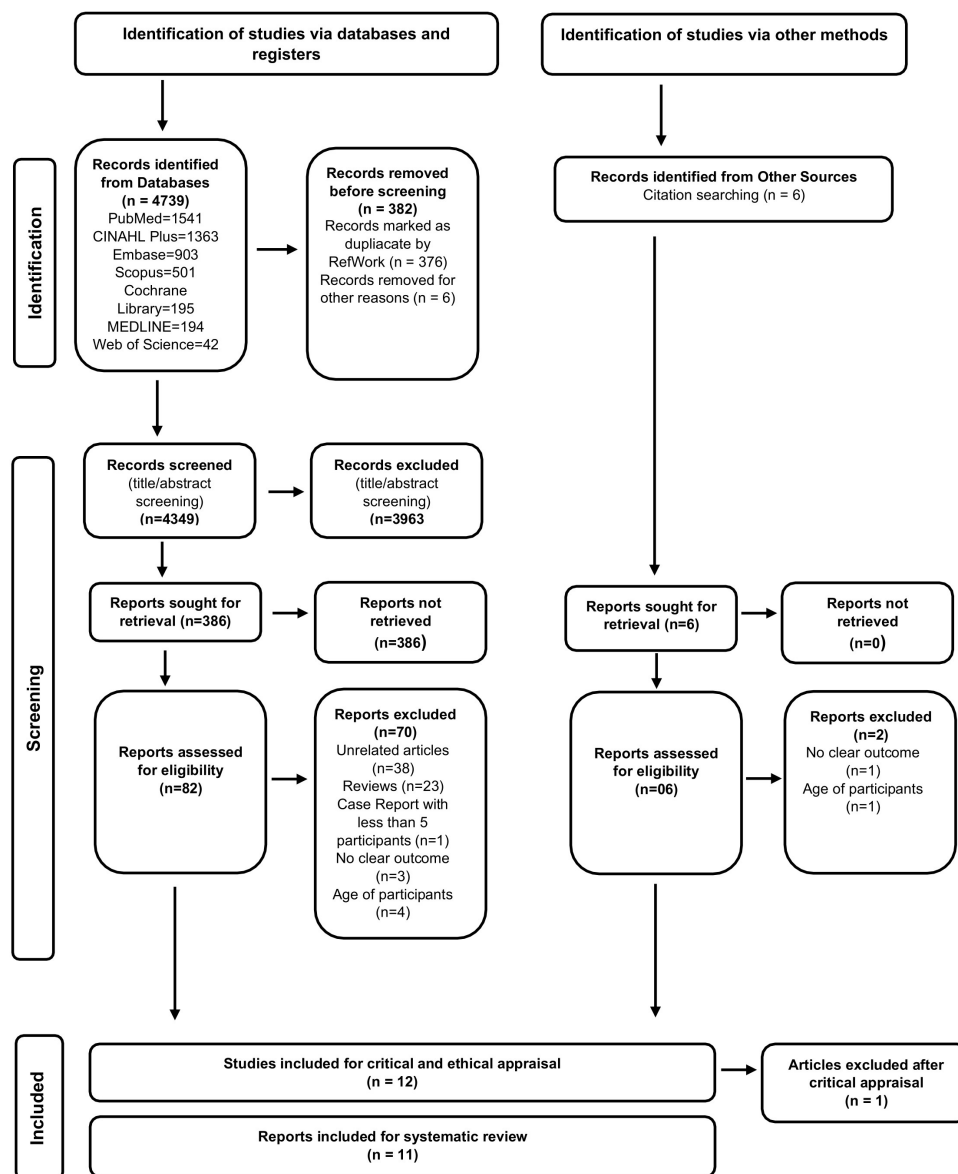


Fig1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement<sup>14</sup>

**Data Abstraction**

Data were extracted from the selected studies in a standardised Microsoft Excel sheet. The following information was extracted: (i) reference (ii) study design (cross-sectional, prospective, retrospective; single centre or multicentre) (iii) study context (clinical setting in which the study was performed) (iv) study period (duration of the study) (v) characteristics of the study population (sample size, health condition) (vi) parameters related to blood transfusion (transfused blood product, primary and secondary outcomes) (vii) aim of the study (viii) results and limitations of the study.

**Analysis**

This systematic review comprises data from quantitative non-interventional observational studies. Since the study subject was broad, this evaluation includes papers with various aims and methodologies. It contains six cohort studies, two case-control studies and three cross-sectional studies. Clinical diversity in aspects of PICO is vast in these studies. The population of all studies includes children below 18 years, but the condition of the population is different (immunocompromised, critically ill children, children after surgery) in each study. Likewise, blood products (plasma, platelet, RBC) transferred in each study were different, and the outcomes were also diverse, from mortality to nosocomial infections. A high degree of heterogeneity precluded meta-analysis, and the information was synthesised narratively.

## Results

### **Study characteristics**

There were 11 prospective and retrospective observational studies included in the study from various regions throughout the world. Three studies from the USA are single-centre studies [20-22]. 2 studies from Canada are also in a single clinical setting [23,24]. Other single-centre studies are from France [25], Brazil [26], Venezuela [27] and Taiwan [28]. One study from the USA used a multi-institutional registry [22], and another study was conducted in three hospital settings [29]. Another international multicentre study was conducted in 82 PICUs of 16 countries [30]. One study [25] is exclusively for infants below one year, and one study [28] is regarding Extremely low birth weight (ELBW) babies. All nine other studies included children up to 18 years. Two studies were about platelets transfusion [20, 30], two studies were about plasma transfusion [23, 25], and one study discussed all the components of blood [26]. The remaining studies were about RBC transfusion [21, 22, 24, 27-29].

All the studies examined the association between blood product transfused (RBC/platelet/plasma) and the adverse outcome in children or infants. Mortality as the worst outcome was discussed in 5 studies [20, 21, 28-30]. Some studies assessed the association between nosocomial infections and other infections in the post-transfused period [23-25, 27, 28]. Other adverse events reported by various studies include intestinal and neurologic complications [20], new or progressive multiple organ dysfunction syndrome [24] (NPMODS), hypotension, systematic inflammatory response syndrome, acute respiratory distress syndrome [21, 24], prolonged PICU stay [23, 30], venous thromboembolism [22], Necrotizing Enterocolitis (NEC), Retinopathy of prematurity (ROP), bronchopulmonary dysplasia (BPD), late-onset sepsis [28], and Transfusion Associated hyperkalemia [29] (TAH).

### **Narrative Synthesis:**

As a result of the narrative synthesis that was performed, the following eight clusters were generated:

01. Platelet transfusion safety
02. Plasma transfusion safety.
03. RBC transfusion safety.
04. Oncology patients under 18yrs.
05. Critically ill children admitted to PICU
06. Injured children less than 15yrs
07. Children underwent surgery
08. Transfusion in infants less than one-year-old
01. **Platelet transfusion safety**

The findings of the investigations on platelet transfusion included information on mortality. One case-control research [20] found that only one fatality occurred among children who had a platelet transfusion, compared to three deaths among children who did not get a platelet transfusion. The child who died in the platelet transfusion group (cases) had a significant neurologic and gastrointestinal compromise, which was the cause of his death. In contrast, the three deaths among children who did not get a platelet transfusion were caused by neurological issues, with one fatality also being related to serious digestive difficulties, according to the findings [20]. The researchers also looked at serious organ involvement events before and after surgery in individuals who received a platelet transfusion vs those who did not. There were no statistically significant differences between the groups noted in the study. The study's principal finding showed no clear differentiation in the severity of acute Post-diarrheal Haemolytic Uremic Syndrome (D + HUS) between children who got platelet transfusions and those who did not [20]. Contrary to this study, another multicentre investigation [30] found that the total platelet dosage provided was independently related to higher ICU mortality. Overall, ICU mortality was 25% but ranged from 18% to 35% depending on the reason for transfusion [30]. Most platelet transfusions were administered to nonbleeding kids as a preventative measure, and platelet thresholds vary significantly [30].

#### **02. Plasma transfusion safety.**

This review includes two papers that look at the consequences of plasma transfusion. The first was a single-centre observational study [25]. It investigates the assumption that plasma transfusion following cardiac surgery is connected with the development of Nosocomial infections (NI) throughout the patient's PICU stay. Plasma transfusion following cardiac surgery with Cardiopulmonary Bypass (CPB) was not shown a significant association for the development of NIs in children younger than one year old who were hospitalised in the PICU [25]. But another single-centre study analyses the association between plasma transfusions and clinical outcomes of critically ill children [23]. The findings show a substantial and independent link between plasma transfusions and higher morbidity [23]. The study showed that patients who received at least one plasma unit had a substantially increased risk of having new or worsening Multiple Organ dysfunction syndrome (MODS), developing hospital-acquired infections, and spending more time in the PICU [23].

### 03. RBC transfusion safety

The transfusion of red blood cells (RBCs) is the most frequent blood product transfusion. This review examined six research for their findings on RBC transfusion in children. RBC transfusion has been associated with worse results in all of the studies. The findings of a study conducted to determine the adverse effects of RBC transfusion in a multidisciplinary PICU population revealed an independent association and a dose-effect relationship between RBC transfusion and increased morbidity [24]. It includes an increased risk of NPMODS, a more prolonged PICU stay, and an increased duration of mechanical ventilation [24]. RBC transfusion was identified as an independent risk factor for nosocomial infections in medical and surgical care centres that provided treatment to critically sick children in another research [27]. According to another study conducted among juvenile trauma patients, early pRBC transfusion was related to a 50% increase in death [21]. Compared to individuals who did not get pRBC transfusion, those who received it late had more extended ICU stays and more ventilator days [21]. When RBC transfusion is performed during surgery, there is an elevated risk of postoperative VTE in paediatric patients; however, this risk is still shallow [22]. A study [28] concluded that the administration of RBCs to ELBW newborns was shown to be related to an increased risk of neonatal mortality. It also established a relationship between RBC transfusion and a higher likelihood of ROP threshold [28]. However, this research found that RBC transfusion positively influenced late cognitive development in ELBW babies, as measured by the MDI score at 18-24 months corrected age in ELBW infants [28]. The frequency of TAH in children who had RBC transfusions was modest (0.93 percent, suggesting that 1 out of every 108 kids in the study developed TAH); nonetheless, the 1-day death rate was 20% in this group of children [29]. A multitude of circumstances caused TAH, and all of the patients in that study had comorbidities that might increase TAH and associated complications [29].

### 04. Oncology patients

The transfusion response profile of paediatric oncology patients was investigated in a study. 55.5% of patients with transfusion reactions were between the ages of 10 and 18, 94.4% were poly-transfused, and 62.3% had no previous history of a transfusion reaction [26]. The transfusion profile showed a high prevalence of urticaria, erythema, and fever, as well as acute allergic-type reactions associated with platelet transfusion [26]. The research also indicated that if they detect a transfusion response, they should promptly cease the transfusion and act to prevent the complication [26].

### 05. Critically ill children admitted to PICU

A study in severely ill children found a substantial and independent link between blood product (plasma) transfusions and higher morbidity [23]. One study [24] reported that RBC transfusions in severely sick infants were related to extended mechanical ventilation and PICU duration. The study further [24] doubts the capacity of preserved RBCs to enhance oxygenation in critically unwell infants. Outcomes such as mortality and NI has also shown an association with blood transfusion in two studies [27, 30].

### 06. Injured children

Among children younger than 15 years of age, three-year research looked into the relationship between transfusion and increased morbidity and mortality in wounded children [21]. A pRBC transfusion was given to 8% of the injured kids (43/512). Approximately one-half of injured children who had an early pRBC transfusion died; nevertheless, most deaths were caused by injuries to the central nervous system [21]. The number of days spent on the ventilator and in the critical care unit was higher in children who had pRBC transfusions than those who did not [21]. In this study, uncontrolled bleeding and coagulopathy were associated with early post-injury mortality following pRBC transfusion [21].

### 07. Children underwent surgery

According to the findings of one research, the use of perioperative RBC transfusions in paediatric surgical patients was related to an increased incidence of postoperative VTE [22]. This relationship remained significant despite accounting for other potential prothrombotic risk factors [22]. In children who have surgery and need RBC transfusions during the surgery, this study says they should be closely watched and given a lower threshold for mechanical and chemical prophylaxis [22]. Children younger than 1 year old who had heart surgery and received plasma had a higher risk of getting bloodstream infections, mediastinitis, and other infections in the hospital [25]. The study was only done at one location [25], making the findings less generalisable. The choice to deliver plasma transfusions in children who underwent cardiac surgery was left to the discretion of physicians on a patient-by-patient basis, and there was no standardisation in this regard [25].

### 08. Transfusion in infants less than one-year-old

Blood transfusion is frequently regarded as a life-saving intervention in highly sick neonates. Most blood transfusions are given to the tiniest and most immature newborns [28]. Hospital mortality and short-term morbidity have been linked to RBC transfusions in neonates [28]. However, in ELBW preterm newborns, the relationship was beneficial in later neurodevelopmental outcomes [28]. In another centre, plasma transfusion following heart surgery in babies younger than one year of age was shown not to affect the outcomes of the patients [25].

## Discussion

A total of 11 papers were found in this systematic review that documented safety associated with different blood product

Transfusion practices in children. The objective of this research was to provide a comprehensive overview of all documented concerns to understand better the clinical adverse reactions and associations linked to blood transfusions.

### Paediatric patients' reactions to blood products

The paediatric patient's reaction to various blood products is different in different contexts. The transfusion outcome depends on the comorbidities and the patient's current health condition. This review noted that the blood transfusion led to mortality, nosocomial infection, MODS, venous thromboembolism, NEC, ROP, BPD, and late-onset sepsis. TAH was seen in individuals who also had other concomitant conditions. In addition to these, intestinal and neurological complications, prolonged ICU stay and 28-day mortality, hypotension, systemic inflammatory response syndrome, and acute respiratory distress syndrome were noted as secondary outcomes.

### Need of long-term studies in the vulnerable population

The review establishes an association between harmful outcomes and children exposed to RBC, platelet and plasma transfusion practices. On the contrary, two studies could not show an association (plasma and platelet) with the outcomes [20, 25]. There were no statistically significant differences in various adverse effects between children exposed to blood transfusion procedures and those not exposed to it [31]. However, the risks of bias revealed in many research and the lack of consistent reporting and definitions of occurrences restrict the conclusions that can be drawn from these investigations.

Blood transfusions are associated with worse outcomes in critically ill children. In severely ill children, plasma and platelet transfusions are related to increased organ failure and death. Despite the possibility of therapeutic advantages, haemostatic transfusions are accompanied by poorer clinical results in the long run. Platelet transfusions were the most often related to transfusion responses in adult and paediatric groups, followed by RBC transfusions and then plasma transfusions [6]. When comparing the paediatric population to the general adult population, there is an overall rise in transfusion responses.

The transfusion profile of oncology patients showed a high prevalence of urticaria, erythema, fever, and acute allergic-type reactions associated with platelet transfusion [26]. Other studies supported these findings. Allergic responses to platelets and RBCs were the paediatric group's most often testified reaction forms. A higher than threefold increase in the rate of allergic reactions to platelets was seen in children than in adults, and a greater than sevenfold increase in the incidence of allergic reactions to RBCs was observed in children compared to adults [7]. According to the findings of this investigation, critically ill children are more prone than adults to respond to blood products, with RBC and platelet transfusions being linked with the most significant magnitude of observed differences. Long-term studies in the vulnerable population (immune-compromised and critically ill children) should be encouraged to reduce the worst outcome.

### Long-term effects of blood transfusion reaction in children

Metabolic complications of blood transfusion remain unnoticed on some occasions. Because young children may have difficulties communicating their symptoms to healthcare practitioners, this finding may be explained by the fact that the clinician must define the reaction solely based on physically visible signs. Transfusion-associated Hyperkalaemia may be more prevalent in juvenile populations, which fall into this category. The frequency of TAH in children who had RBC transfusions was modest, and a multitude of circumstances caused TAH [29]. It could also be a sign that medical staff would be too careful when giving RBC products to children, leading to a reaction report that doesn't meet any case definition criteria [7].

According to the findings of one research, the use of perioperative RBC transfusions in paediatric surgical patients was related to an increased incidence of postoperative VTE [22]. Another study [32] confirmed by confirmed that children, infants, and neonates who get preoperative RBC transfusions are more likely to have new or worsening VTE after surgery [32]. Another study also observed various transfusion reactions over two years in a PICU in a study and noted increased mortality [33]. There are no studies with a well-developed follow-up or information on the long-term consequences of blood transfusions in children. Improvements in the observation of transfusions administered to patients in the PICU and improved understanding of these responses among healthcare workers should help to enhance the safety of transfusions in the PICU.

### Various alterations to familiarise and standardise children's adverse transfusion reaction

This review noted that post-surgical children who needed blood transfusion should be closely watched and given a lower threshold for mechanical and chemical prophylaxis [22]. An additional risk factor related to RBCT is the duration of the procedure, haemorrhage, and oxygen saturation levels. These considerations should be considered when planning paediatric treatments, particularly where exposure to RBCT is desired [34]. De Pascale, et al., reported that apheresis of platelet and RBC showed more excellent transfusion safety [35]. Other studies also supported blood product modification. Modifications to blood products can significantly reduce the dangers associated with transfusions [3]. They have also proposed leukoreduction, irradiation, washing, volume reduction, pathogen inactivation, and other treatments [3]. Alteration of the blood product can improve transfusion safety by reducing the risk of infection. More research, however, is needed to determine the safety of each alteration for each kind of blood product in question. Every alteration is unique, and it will behave uniquely with each and every blood product.



### Develop new health data and strategies to increase the safety

A significant incidence of transfusion reactions in children is seen, which depends on the following variables: the kind of blood component administered, patient comorbidity, and the number of transfusions received; the sort of response is also connected with the type of blood component and the age of the patient [36]. The understanding of patients and the variables that contribute to transfusion responses serve as the foundation for the development of preventative measures, which ultimately contribute to improving the transfusion services and care provided to patients.

It is estimated that current transfusion practices partially comply with suggested transfusion standards. Guidelines for transfusions in children are based primarily on "professional opinion" instead of scientific proof. Likewise, to adult transfusion methods, present transfusion practises in children frequently do not reflect the application of existing knowledge about the necessity for transfusion. More extraordinary efforts to implement current evidence-based transfusion practices are needed. New health data and strategies should implement to increase the safety from adverse transfusion reactions in young children

### **Limitations of the study**

Given several studies identified, the research quality that has provided primary and secondary outcomes has been low. Numerous studies were likely to have been compromised by confounding due to indication bias. More severely sick babies were more likely to have a blood transfusion than the rest of the population. Furthermore, the sample sizes in many research are from a single centre, which is insufficient for addressing damage comprehensively. This review included only articles published in English, which might give rise to selection bias. Some reports did not mention the age of the children and those articles were skipped from the review. Data from those articles might contribute to reasonable interpretations. This review included studies with the retrospective/prospective nature of the data analysis. These descriptive studies can reveal an independent association, but they cannot prove a cause-and-effect relationship between blood transfusions and outcomes in children. Only a randomised clinical trial can definitively prove the existence of a cause-and-effect relationship between blood transfusions and outcomes in children.

## Conclusion

Acute and chronic diseases usually necessitate blood transfusions. This systematic study emphasises paediatric transfusion responses and shows that the incidence of transfusion reactions among the paediatric population is on the rise. The findings of this review indicate that further clinical studies with specified criteria for adverse events are required to settle the uncertainty surrounding the safety of blood transfusion in a population with relative immunologic immaturity. Even though the current data do not support the safety of transfusion triggers, they do highlight the significance of future investigation. Performing a randomised trial with a bigger number of patients, in my opinion, would be beneficial in order to recommend other techniques for establishing more precise criteria for preventing hazardous acute responses in paediatric patients who are transfusion dependent. The need for more research to explain suitable indications and the introduction of standardised protocols for the blood transfusion process and subsequent reactions in critically sick children are considered necessary.

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None

### **Ethical Considerations**

None

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### **Author contribution statement**

**Ancy Chandrababu Mercy Bai**: Conceptualization (lead); writing – original draft (lead); formal analysis (lead); writing – review and editing (equal). **Divya Vinnakota**: conceptualization, Software (lead); writing – review and editing (equal). **Abu Rushd Mohammad Mashrur**: conceptualization, Resources; writing – review and editing (equal). **Sumana Choudhury**: conceptualization, Software (lead); writing – review and editing (equal). **Ajoy Kumer Ghosh**: conceptualization, Software (lead); writing – review and editing (equal). **Russell Kabir1**: Conceptualization (lead); writing – original draft (lead); formal analysis (lead); writing – review and editing (equal).

### **Data availability statement**

Data included in article/supp. material/referenced in article.

### **Additional information**

No additional information is available for this paper.



**Declaration of competing interest**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Russell Kabir is an author of this paper. Therefore, the peer review process was managed by alternative members of the Editorial Board and the author had no involvement in the decision-making process.

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